

Reprinted from the American Journal of Physiology.

VOL. XXIX. — DECEMBER 1, 1911. — No. II.

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AND SENSORY STIMULATION ON  
ADRENAL SECRETION.

By W. B. CANNON AND R. G. HOSKINS.

[FROM THE LABORATORY OF PHYSIOLOGY IN THE HARVARD MEDICAL SCHOOL.]



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## THE EFFECTS OF ASPHYXIA, HYPERPNŒA, AND SENSORY STIMULATION ON ADRENAL SECRETION.

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[From the Laboratory of Physiology in the Harvard Medical School.]

IN order that experimental results shall be reliable, it is necessary that the effects of common experimental conditions themselves shall be understood. A failure to regard these immediate effects of interference with organic processes has been a noteworthy source of error in the history of experimental biology. With the purpose of learning whether the artificial production of asphyxia, or the presence of hyperpnœa, or the stimulation of sensory nerves would affect the secretion of epinephrin, the present investigation was undertaken.

Since the procedures utilized required the use of a general anæsthetic, one must be employed which is not attended by increased adrenal activity. Without studying the influence of various general anæsthetics on adrenal secretion, — which will be the aim of another research, — we followed in the main the procedure described by Elliott<sup>1</sup> and found that urethane dissolved in a small amount of water and given, 2 gm. per kilo body weight, by stomach, to cats and rabbits, produced satisfactory general anæsthesia, free from any stage of excitement which might stimulate the adrenal glands, and in fact unattended by any increase of adrenal secretion demonstrable by our tests.

The method of testing for epinephrin in the blood was the modification of the intestinal strip method suggested by Hoskins,<sup>2</sup> — the use of segments of rabbit intestine, suspended lengthwise in a glass cylinder through which oxygen was passed. The segment, when not surrounded by the blood to be tested, was bathed in Ringer's solution

<sup>1</sup> ELLIOTT: Journal of physiology, 1905, xxxii, p. 448.

<sup>2</sup> See HOSKINS: Journal of pharmacology and experimental therapeutics, 1911, iii, p. 95.



at body temperature. If a rabbit is anæsthetized with urethane, it will supply the highly sensitive fresh segments as they are needed. The animals experimented on were cats. Rabbit's intestine was proved to be quite as sensitive to a minute amount of adrenalin in cat blood as in rabbit blood. The innocuousness of cat blood for the rabbit intestine is shown by the prolonged rhythmic contraction of the rabbit intestine in that blood. The blood to be tested was taken before and after the experimental procedures by catheterizing the inferior vena cava, as described by Cannon and de la Paz.<sup>3</sup> Care was taken in all instances to insert the catheter to the same point anterior to the entrance of the adrenal veins, and to place the catheter opening (which was at one side) always in the same position relative to the wall of the vein.

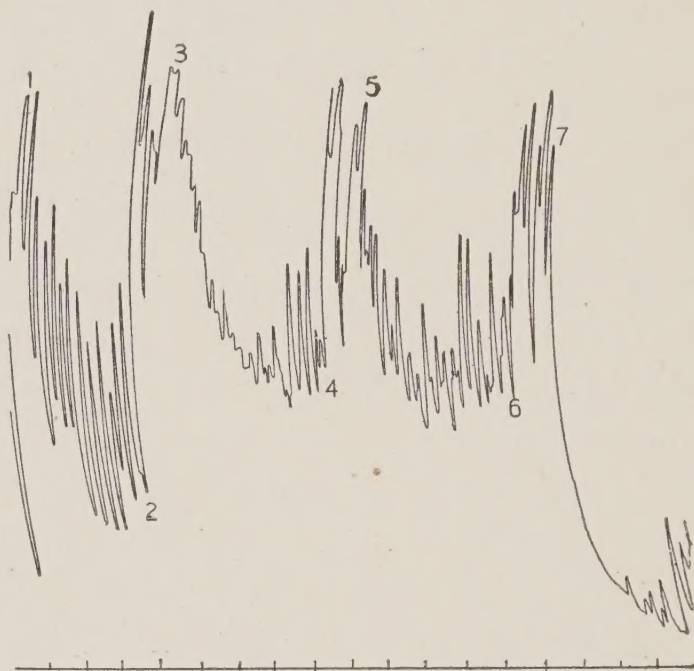


FIGURE 1. — Effect of asphyxia on adrenal secretion. At 1 normal vena cava blood applied, at 2 removed. At 3 normal blood from femoral vein applied, at 4 removed. At 5 blood from femoral vein after asphyxia applied, at 6 removed. At 7 blood from the vena cava after asphyxia applied. Time, half-minutes.

**The effect of asphyxia.** — The effect of asphyxia was tested by comparing the action of blood, taken as nearly simultaneously as possible from the vena cava and the femoral vein before asphyxia, with blood taken from the same sources after asphyxia had been produced. The femoral venous blood after passing the systemic capillaries thus acted as a standard for the same blood after receiving the contribution of the adrenal veins. Asphyxia was caused by covering the tracheal cannula until respiration became labored and slow, but capable of recovery when air was admitted. It may be regarded, therefore, as not extreme.

The results of the degree of asphyxia above described are shown

<sup>3</sup> CANNON and DE LA PAZ: This journal, 1911, xxviii, p. 64.



graphically in Fig. 1. Blood taken from the vena cava and from the femoral vein before asphyxia ("normal") failed to cause inhibition of the contractions. Blood taken from the femoral vein after asphyxia produced almost the same effect as blood from the same vein before; asphyxia therefore had wrought no change demonstrable in the

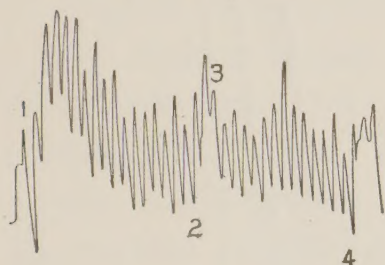


FIGURE 2. — Failure of hyperpnea to cause increased adrenal secretion. At 1 normal blood from vena cava applied, at 2 removed; at 3 blood from vena cava after hyperpnea applied, at 4 removed. Time, half-minutes.

general venous flow. Blood taken from the vena cava after asphyxia had, on the contrary, an effect markedly unlike blood from the same region before, — it caused the typical inhibition which indicates the presence of adrenal secretion.

This positive result might suggest that the comparison of both femoral and vena cava blood under each condition was unnecessary, and that a comparison merely of vena cava blood before and after asphyxia would be sufficient. Positive results were indeed thus secured, but they occurred even when the adrenal glands were carefully removed and extreme asphyxia (*i. e.*, stoppage of respiration) was induced. That the blood may contain in extreme asphyxia a substance or substances capable of causing inhibition of intestinal

contractions was thus demonstrated. In one instance, after the blood was proved free from epinephrin, the aorta and vena cava were tied close below the diaphragm, and the carotids were tied about midway in the neck. Extreme asphyxia was produced (lasting five minutes). Blood now taken from the heart caused marked inhibition of the beating intestinal segment. Probably, therefore, the inhibitory action of blood taken from an animal when extremely asphyxiated cannot be due to epinephrin alone.

That the positive result obtained in moderate asphyxia, on the other hand, is not attributable to other agencies in the blood than epinephrin, is indicated by the failure of asphyxial femoral blood to cause inhibition, while vena cava blood, taken almost simultaneously, brought about immediate relaxation of the muscle.

The conclusion is justified, therefore, that asphyxia results in increased secretion of the adrenal glands.



**The effect of hyperpnœa.** — It is known that some bodily conditions, such as rapid heart beat and glycosuria, may occur during acapnia as well as during certain stages of asphyxia.<sup>4</sup> It was possible, therefore, that hyperpnœa, like asphyxia, would be accompanied by adrenal secretion.

Hyperpnœa was caused by opening the chest of the anæsthetized animal along the mid-sternal line, and holding the chest walls apart while the lungs were inflated in rapid repetition by means of bellows. The air forced into the lungs was permitted to escape quickly through an opening in the trachea. The method is only slightly modified from that used by Henderson in producing acapnia. Artificial respiration was continued in some instances for five minutes, and, in the instance which gave the record reproduced in Fig. 2, for ten minutes. Such artificial respiration would be followed by apnœa lasting for more than a minute.

As Fig. 2 indicates, the hyperpnœa caused by artificial respiration is not attended by any increase of adrenal secretion — the blood before and after the process has almost the same effect on the intestinal neuromusculature. In other instances than that represented in Fig. 2 the blood after hyperpnœa caused less relaxation than normal blood from the same animal, when applied after Ringer's solution to the beating intestinal segment. The suggestion might be offered that the greater oxygen content of the blood would favor more

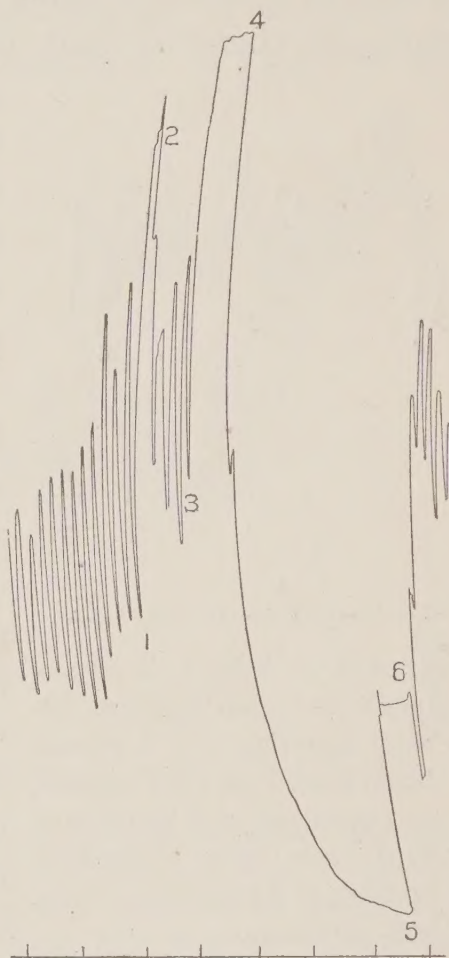


FIGURE 3. — Effect of sensory stimulation on adrenal secretion. Intestinal segment beating in normal vena cava blood, removed at 1 and renewed at 2. At 3 normal blood removed. At 4 vena cava blood after sensory stimulation applied, at 5 removed. At 6 Ringer's solution applied. Time, half-minutes.

<sup>4</sup> See HENDERSON: This journal, 1908, xxi, p. 146; HENDERSON and UNDERHILL: This journal, 1911, xxviii, p. 287.



rapid oxidation of epinephrin, and that thus an increased secretion might be masked. That this explanation is improbable is indicated by the persistence of epinephrin in the blood when pure oxygen is permitted to bubble through it for much longer than ten minutes. It is altogether likely, therefore, that hyperpnœa, to a degree resulting in acapnia, is not attended by increased adrenal secretion.

**The effect of sensory stimulation.**—Stimulation of sensory fibres in one of the larger nerve trunks is known to result in discharges along sympathetic paths. Thus such stimulation causes dilatation of the pupils, inhibition of gastric peristalsis and gastric secretion, and contraction of arterioles. Since the adrenal glands are stimulated to activity by sympathetic impulses, it was possible that they would be affected like some of the other organs innervated by the sympathetic system, and secrete in greater abundance when sensory nerves were irritated.

The sensory stimulus, applied to the sciatic nerve of the anæsthetized animal, was a tetanizing current which was increased in strength as the period of stimulation progressed, so that the pupils were kept dilated. Probably the stimulus used was much stronger than would be necessary to obtain a positive result in the absence of urethane, for Elliott found that urethane markedly lessens conductivity or irritability of visceral nerve fibres.<sup>5</sup> In different instances the stimulation lasted from three to six minutes. Throughout the period there was marked hyperpnœa.

As Fig. 3 shows, the normal blood, removed from the vena cava before stimulation, caused no inhibition of the beating segment, whereas that removed afterwards produced a marked relaxation. Since hyperpnœa does not result in an augmented adrenal activity, we may conclude that the adrenal glands are affected through nervous channels when a sensory trunk is strongly excited, and that under these circumstances they pour into the blood stream an increased amount of secretion.

The similarity between surgical shock and the condition of an animal after removal of the adrenal glands suggests that possibly in surgical shock the injury to large nerve trunks may discharge the adrenal glands to such a degree that they are unable to continue their

<sup>5</sup> ELLIOTT: *Loc. cit.*, p. 448.

normal functioning. Hesitating to add another to the already numerous theories of surgical shock, we merely wish to point out that since sensory stimulation causes increased adrenal secretion, adrenal fatigue or exhaustion may reasonably be regarded as an element in the complex.















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